CENTERS FOR DISEASE CONTROL

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Severe Neutropenia during Pentamidine Treatment of *Pneumocystis carinii* Pneumonia in Patients with Acquired Immunodeficiency Syndrome — New York City

During November 1983, three patients at one New York City hospital who had the acquired immunodeficiency syndrome (AIDS) and *Pneumocystis carinii* pneumonia (PCP) developed severe neutropenia while being treated with pentamidine isethionate. Since August 1981, 23 other patients with AIDS and PCP had been treated with pentamidine at this institution. None developed neutropenia that could not be explained by the simultaneous administration of another drug.

Case 1: A 43-year-old male with recently diagnosed Kaposi's sarcoma (KS) was suspected of having PCP in late October 1983, based on symptoms of cough, dyspnea on exertion, a chest roentgenogram showing bilateral interstitial pulmonary infiltrates, and pulmonaryfunction tests showing a drop in arterial p0, with exercise. He was begun on sulfamethoxazole/trimethoprim (SXT) (20 mg trimethoprim/kg/day orally) as an outpatient. Before treatment, his white blood cell count (WBC) was 5,700/mm3 (4,560 neutrophils/ mm3). After 9 days of SXT, he developed a maculopapular rash, an elevated serum glutamicoxaloacetic transaminase (SGOT), an elevated serum creatinine, and neutropenia (WBC = 1,700/mm3 with 816 neutrophils/mm3). SXT was discontinued. The patient was admitted to the hospital 4 days later. Toluidine-blue and Gram-Weigert stains of a bronchoalveolar lavage showed P. carinii cysts, and the patient was started on pentamidine isethionate 4 mg/kg/day intravenously.* Two days before pentamidine was started, his WBC was 2,700/mm3 (1,377 neutrophils/mm³) but rose to 4,000/mm³ at initiation of pentamidine. All other manifestations of SXT toxicity had resolved. The patient's WBC ranged between 3,200/mm3 and 5,600/mm3 during the first 5 days of treatment. He experienced transient flushing during the treatment infusion, which disappeared when the infusion time was increased from 45 to 90 minutes. On day 6 of pentamidine, he developed a fever but no thrombocytopenia or anemia. His WBC was 1,900/mm3 and dropped to 300/mm3 (36 neutrophils/mm3) on day 7. The drug was discontinued, and gentamicin plus moxalactam were begun. During the 10 days after discontinuation of pentamidine, his WBC rose gradually to 2,800/mm3 (868 neutrophils/ mm3), and a bone-marrow aspirate showed an increased myeloid to erythroid stem-cell ratio.

^{*}Since intravenous administration of pentamidine can be hazardous, CDC recommends that it be given intramuscularly whenever possible.

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Neutropenia - Continued

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The patient received no further therapy for PCP, and a repeat bronchoalveolar lavage revealed no *P. carinii*. His respiratory symptoms improved markedly. However, *Mycobacterium avium-intracellulare* was found in a blood culture that had been taken in late October, and the patient was treated with ansamycin. During the first 4 days of ansamycin, his WBC ranged from 2,800/mm³ to 4,300/mm³ (neutrophils 868 mm³ to 1,785/mm³) but fell to 1,900/mm³ on day 5 when the drug was discontinued. The following day, his WBC was 1,500/mm³, with 405 neutrophils/mm³. Five days later, the patient was discharged with a WBC of 1,500/mm³. Thereafter, he remained well, and during the 25 days after discharge, his WBC rose gradually to 2,200 mm³.

Case 2: A 30-year-old male, referred for diarrhea and started on tetracycline as an outpatient, was admitted with fever, dyspnea, abnormal chest roentgenogram, and abnormal pulmonary-function tests. P. carinii cysts were seen on toluidine-blue and Gram-Weigert stains of a bronchoalveolar lavage, as well as on a methenamine-silver stain of a transbronchial biopsy and a Gram-Weigert stain of bronchial brushings. Vibrio parahemolyticus and Giardia lamblia were found in his stool. He was begun on SXT (20 mg trimethoprim/kg/day intravenously) and tetracycline. After 8 days of SXT, he developed a rash, and his WBC fell from a pretreatment level of 5,400/mm3 (3,888 neutrophils/mm3) to 1,900/mm3. SXT and tetracycline were discontinued. The following day, his WBC was 1.800/mm3, with 1.026 neutrophils/mm3. Over the next 4 days, the rash disappeared, and his WBC rose to 2,900/mm3 (2,175 neutrophils/mm3). The patient was then started on pentamidine isethionate 2 mg/kg/day intravenously, which was increased to 4 mg/kg/day after 2 days. During the first 6 days of pentamidine, his WBC rose to 4,300/mm3 but then gradually fell to 1,700/mm3 (980 neutrophils/mm3) by the 11th day of therapy. Pentamidine was discontinued, and his WBC fell to 1,600/mm3 2 days later. He did not develop anemia or thrombocytopenia. However, his respiratory status had improved markedly, and he was discharged from the hospital. Quinacrine was begun for his Giardia infection as an outpatient. After 7 days, his WBC rose to 2,800/mm3. He remained clinically well 2 weeks after all therapy was discontinued.

Case 3: A 29-year-old male was admitted with a history of fever and dyspnea for 2 weeks. P. carinii cysts were seen on a Gram-Weigert stain of a bronchoalveolar lavage. Since the patient gave a history of a diffuse pruritic rash when treated with SXT in August 1983 for an upper respiratory infection, he was started on pentamidine isethionate 4 mg/kg/day intravenously at the outset. With each infusion of the drug, he developed hypotension, flushing, and chills, which were controlled by increasing the infusion time from 1 to 3 hours and by pretreatment with meperidine and diphenhydramine. His WBC before pentamidine administration was 1,300/mm3 with 910 neutrophils/mm3. His WBC initially was stable but fell from 1,400/mm3 on day 6 to 500/mm3 (55 neutrophils/mm3) on day 7. He developed a fever and was placed on gentamicin and ticarcillin. The following day, with a WBC of 400/mm3 (8 neutrophils/mm3), pentamidine was discontinued. Throughout this period, the patient did not develop anemia or thrombocytopenia. He was begun on SXT (15 mg trimethoprim/kg/day intravenously); the drug was continued for 11 days, during which his WBC rose to 1,700/mm3. SXT was well tolerated, except for mild pruritis and an erythematous rash that disappeared when the drug was stopped. His chest film and respiratory symptomatology had improved markedly. The patient was discharged 12 days later and remained well at a followup appointment 7 days thereafter.

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Neutropenia - Continued

Editorial Note: For each patient, this was the first admission for PCP, and each showed clinical recovery. In two, recovery occurred while on pentamidine therapy. Folinic acid, topical antifungal agents, benzodiazepines, and in one patient, meperidine and diphenhydramine, were administered during the period in which the pentamidine-associated neutropenia developed. Furthermore, despite intensive screening, only a few other infectious agents (*G. lamblia*, *V. parahemolyticus*, *M. avium-intracellulare*, and superficial *Candida*) complicated these cases. In two of these, neutropenia developed or worsened during the administration of other anti-infective drugs. Thus, despite the close temporal relationship between neutropenia and the administration of pentamidine and the gradual improvement of the neutropenia after withdrawal of the drug, it should not be presumed that these reactions were specifically related to pentamidine.

CDC's Parasitic Diseases Drug Service has received standard report forms for 179 patients with AIDS and PCP treated with pentamidine from January 1982 to September 1983. Of these, 26 (14.5%) developed leukopenia, with decreases in leukocyte counts from pre-therapy to mid- or post-therapy of 50% or more. In 12 instances, the physician discontinued pentamidine because of leukopenia, and in six of these 12, neutropenia or granuocytopenia was specifically mentioned as a complication. However, standard report forms ask only for WBC and are otherwise not sufficient to further characterize this phenomenon. CDC has sent a questionnaire to physicians for 114 randomly selected patients for whom pentamidine was released from October 1, to December 16, 1983, to obtain a more complete characterization and incidence estimate. In addition, physicians using pentamidine are encouraged to provide more detailed information on hematologic changes occurring during pentamidine treatment on the standard patient report form for pentamidine therapy.

International Notes

Lung Cancer among Women - Canada

From 1932 to 1981, the age-standardized mortality rates (ages 25-74 years) for lung cancer among Canadian women increased from 2.8/100,000 to 25.1/100,000. This is the most rapidly increasing cancer rate among women, and lung cancer rates for Canadian women have risen from ninth position in 1965 to second in 1981 (Table 1). Since this increase has shown an exponential rise, and breast cancer mortality has tended to decrease (Figure 1), lung cancer can be expected to become the leading cause of cancer death for Canadian women by about 1987. Furthermore, because the lung cancer mortality rates

TABLE 1. Lung and breast cancer mortality ranks and percentage of total cancer among women — Canada

	Lung (Breast Cancer			
Year	Rank	%	Rank	%	
1965	9	4.1	1	20.6	
1966	8	4.4	1	19.9	
1971	5	5.8	1	20.6	
1976	3	8.5	1	20.4	
1981	2	11.9	1	19.8	

Lung Cancer - Continued

among males are gradually slowing, lung cancer mortality rates for females may equal those for males by 2000 (1).

The risk of developing lung cancer is strongly associated with smoking. A survey of smoking habits by the Canada Labour Force showed that changes in smoking habits of Canadian women are related to the increased lung cancer rate:

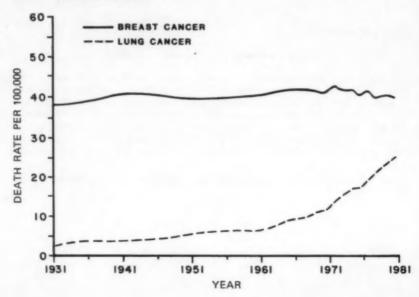
- From 1965 to 1979, the proportion of regular women smokers was constant, but the proportion of heavy smokers (25 or more cigarettes/day) increased continuously.
- In the province of British Columbia, the proportion of heavy smokers rose before other provinces, and was reflected by an earlier trend in the rapid increase of lung cancer mortality among women in British Columbia.

The proportion of heavy smokers in British Columbia remains higher than in the other Canadian provinces and is reflected by a faster increasing rate of lung cancer among British Columbian women than among women in the rest of Canada. In some provinces, the proportion of regular smokers continues to decrease, despite increases in the proportion of heavy smokers and in the average number of cigarettes consumed per day.

Reported in Chronic Diseases in Canada (1983;4:32-4) by Y Mao, H Smith, Non-Communicable Disease Div, Bureau of Epidemiology, Laboratory Centre for Disease Control, Health and Welfare Canada; Office of the Director, Center for Health Promotion and Education, CDC.

Editorial Note: The lung cancer epidemic among women is also occurring in the United States (Figure 2). The American Cancer Society estimates that 36,000 women will die in the United States from lung cancer in 1984. This approaches the 37,300 estimated deaths from

FIGURE 1. Age-standardized (25-74 years) lung and breast cancer mortality rates among women — Canada, 1931-1981



Lung Cancer - Continued

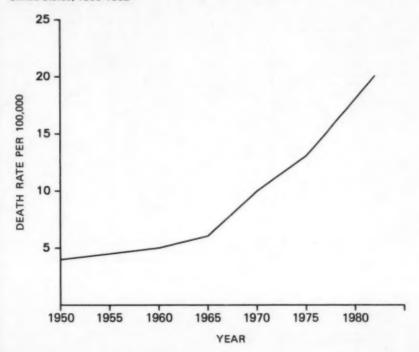
breast cancer, which has been the primary cause of cancer mortality among U.S. women (2). In at least two states, Kentucky and Washington, lung cancer deaths have exceeded breast cancer deaths among women (3.4).

Approximately 85% of all lung cancer cases are attributable to cigarette smoking (5). The lung cancer epidemic is especially tragic because it is preventable, increased focus on the health problems of smoking among women and on the potential for effective intervention is needed (6).

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FIGURE 2. Age-adjusted death rates of respiratory cancer among white women — United States, 1950-1982



Epidemiologic Notes and Reports

Fulminant Hepatitis B among Parenteral Drug Abusers — Kentucky, California

During the first 10 months of 1983, unrelated clusters of fulminant hepatitis B (HB) deaths occurred in Madisonville, Kentucky, and Porterville, California. Both outbreaks were limited to circles of parenteral drug abusers and their sexual contacts. Thirty-six cases occurred, with five deaths, for a case-fatality ratio (CFR) over 10 times the expected ratio.

Investigations involved active HB case finding, identification of possible risk factors for fulminant HB, and serotesting for HB and the Delta agent (a dependent virus recently implicated as a co-factor in fulminant HB infection). In both outbreaks, a case was defined as: (1) acute clinical symptoms compatible with hepatitis B; (2) acute elevation of serum glutamicoxaloacetic transaminase (SGOT) or serum glutamic-pyruvic transaminase (SGPT) two or more times greater than the upper limit of normal; and (3) positive hepatitis B surface antigen (HBsAg) serology.

(Continued on page 76)

TABLE I. Summary-cases specified notifiable diseases. United States

47 51 10 11 13,966	February 12, 1983 N 89 23	Median 1979-1983 N 77	February 11, 1984 304 498	February 12, 1983	Median 1979-1983
10	89			Pá	
10		77	400		N
1	23		480	539	399
1	23				
13,966		17	76	106	97
13,966		2	4	5	11
	17,406	17,693	93,031	108,745	112,172
304	638	552	2.314	3.065	3,205
351	404	442	2.243	2.709	2,709
347	450	371	2,288	2.380	1,912
32	67	N	313	326	N
124	100	163	642	777	1.050
6	11	N	37	60	N
7	6	5	22	31	27
2	21	17	55	73	73
35	12	35	163	52	199
36					N
	6		7		N
54			288		353
	77				352
	1		200		302
62	83	124	244		579
					113
					251
					3,394
7					54
2					N
					2,434
	1	3	1,020		11
			21		35
	1	4		34	30
	93	93		,	517
	54 54	54 78 54 77 52 83 57 23 57 11 513 669 7 19 338 454 3 4	54 78 76 54 77 77 52 83 134 57 23 19 51 1 44 513 669 568 7 9 N 338 454 472 3 4 5 2 1 1	54 78 78 288 54 77 77 288 52 83 134 344 57 23 19 167 5 11 44 42 513 669 568 3.095 7 13 11 40 2 9 N 30 338 454 472 1,920 3 4 5 21 2 1 1 6	54 78 76 288 344 54 77 77 288 348 52 83 134 344 462 57 23 19 167 113 513 669 568 3,095 4,019 7 13 11 44 42 83 7 13 11 40 64 2 9 N 30 52 338 454 472 1,920 2,180 3 4 5 21 34 2 1 1 6 7

TABLE II. Notifiable diseases of low frequency. United States

	Cum, 1984		Cum. 1984
Anthrax Botuliar: Foodborne Infant Other BruceBosis: (Va. 1) Cholers Congenital rubells syndrome Dioththeris	5 1 12	Plague Poliomyeléris: Total Paralytic Paralytic Rabies, human Tetanus (Vs. 1) Trichinosis Typhus fever, flas-borne (andemic, murine)	7 3 2 2

[&]quot;There were no cases of internstionally imported messles reported for this week.

TABLE III. Cases of specified notifiable diseases, United States, weeks ending February 11, 1984 and February 12, 1983 (6th Week)

		Aseptic	Encep	phalitis	Con	norrhea		lepatitis (V	iral), by ty	pe	Legionel-	
Reporting Area	AIDS	Menin- gitis	Primary	Post-in- fectious	IC	ivilan)	A	8	NA,NB	Unspeci- fied	losis	Lepros
	Cum. 1984	1984	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1983	1984	1984	1984	1984	1984	Cum 1984
UNITED STATES	304	51	75	4	93,031	108,745	351	347	32	124	6	22
NEW ENGLAND Maine	15	2	3		3,114	2,654	8	21	1	12		1
N.H.		1	1	-	70	81	1	-				
/t.		-			43	50			1			-
Mass.	8		2		1,094	1,188	5	11		12		1
L.L. Conn.	7	1		-	1,592	1,009	1	8 2	:	-	:	
MID ATLANTIC	174	5	5		11,863	13,708	52	67	2	7		2
ipstate N.Y.		3	1	*	1,869	1,841	13	24	1	4		2
N.Y. City N.J.	158		2	-	5,316	5,704	33	15		3	* 1	
Pa.	16	2	2		1,687	2,713 3,450	6	28	1	:	2	
E.N. CENTRAL	10	7	15	1	11,811	15,354	16	39	3	6	3	1
Office and	7	4	4	1	2,989	4,041	4	25	1	3	1	-
no.	2	i	2	-	1,861	1,683	4	3	2	2	*	
Mich.	1	2	6	-	1,780 3,776	4,005 4,336	6	10	*	1	2	1
Nis.			3		1,405	1,289	1		-			
W.N. CENTRAL	1	3	3		4,475	5,019	16	8		1		-
Minn, owa		i	2	*	627	797	6	2			*	-
Mo.	1	9	2	-	1,992	538 2,318	2	2 4		1	-	-
V. Dak.				-	50	51						
S. Dak.				-	147	144	7					
labr. Cans.		1	1	:	340 750	288 885	:	-	:	-	-	-
S. ATLANTIC	19	14	20	3	24,608	26.527	17	87	11	14		
Del.	1		1		428	574		07		144		
VId.	5	3	3	-	3,370	3,493	1	12	1	2		
D.C.	4	-	-		1,747	1,780			-	-	*	
Va. W. Va.	2	5	7 2	2	2,481	2,423	i	23	3	2	*	1
N.C.		4	1	1	3,955	3,508	4	3	1	4		
S.C.	-		1	-	2.253	2,815	2	13		3		
Ge.		*	2		4,773	4,962	4	13	2	1		
Fla.	7	2	3		5,318	6,681	5	20	4	2		
E.S. CENTRAL Ky.	1	11	3	-	8,097	9,732	36	38	2		1	
Tenn.		*	1		1,014	1,309 3,618	18	22	2		1	
Ala.		7	2		2,600	3.248	13	14				
Miss.			•		1,215	1,557	2	2	-		*	
W.S. CENTRAL	2	5	5	*	13,206	15,402	84	61	3	72	1	
La.		2	1		1,184	2,361	9	22	1	3		
Okla.	. 1	2			1.508	1,832	9	6		4	1	
Tex.	1	1	4	*	7,372	10,031	65	28	1	62	-	
MOUNTAIN Mont.	4	2	1		2,915	3,108	82	16	7	11	1	4
daho	-	1			116	165	1		-		-	
Wyo.					77	99	2					
Colo.					739	882	20	6	3	2		
V. Mex. Ariz.	:	:		*	369	421	11		-		-	
Jtah	4	1	1		766 165	709 149	19 28	3	2	6	1	4
Vev.	-	-	-		527	542		6	i	-		
PACIFIC	78	2	20		12,942	17,241	40	10	3	- 1	-	13
Wesh.	-	-			843	1,061	8	6	1	1	-	1
Oreg. Calif.	78	Ü	20	-	776 10,791	774 14,725	32 U	3	2	ú	Ü	- 1
Alaska	/0	9	20		311	347		1	0			1
Hawaii	-	2	*		221	334		-			-	-
Guam P.R.		U			467	32	U	U	U	U	U	
V.I.		2	-	-	405 54	390	13	13	*	3	-	
Pac. Trust Terr.		Ü			94	30	Ú	Ú	Ü	Ü	Ü	

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending February 11, 1984 and February 12, 1983 (6th Week)

	Malario		Mee	sies (Rut			Menin- gococcal	Mun	200		Pertussis		Rubella			
Reporting Area	HARIBTIO .	Indig	enous	Impo	* bet	Total	Infections	-						_	-	
	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	1984	Cum. 1984	Cum. 1983	
UNITED STATES	55	35	188		7	62	288	52	344	57	167	113	5	42	83	
NEW ENGLAND	5		1		*		14	5	13	1	3	7		1		
Maine		-	i	-	*		2	1	5		1	2	-		-	
N.H. Vt.		-	1	-			2	1	1	1	1	1	-		-	
Maas.	4		-				3	3	6			3		1	*	
R.L.		-			*		3				1	1		*	-	
Conn.	1	*		*			4	-	-		*				-	
MID ATLANTIC	2					1	35	10	65	2	7	21			2	
Upstate N.Y.	1					1	14	1	12		5	11			1	
N.Y. City						*	1		1	*	*	1	*	*	1	
N.J.				*	*	*	. 8	7 2	49	2	2	3			-	
Ps.	1			*		*	12	2	3	4						
EN. CENTRAL	7	11	98			22	50	20	104	20	34	36	*	4	14	
ONio	4			-			21	3	25		5	16	*		1	
lvd.				*	-		6	5	11	19	19	11		3	4	
ML.	1	4	16			17		4	31	i	3 4	11	-	1	2	
Mich.	- 1	7	83	-	-	5	12	8	7		3	5			7	
Wis.	1			-												
W.N. CENTRAL	3				*		26	4	16	3	#2	6	1	3	8	
Minn.		*	*	*			2	1	1		3	2	-		2	
OWS	-	*	*			-	10	2	3	1	1	1	-		-	
Mo.	2			*		-	9	1	-				-	1		
N. Dak. S. Dak.	-			-			1									
Nebr.							2		1	-						
Kans.	1	*					2		7	3	36	3	1	2	6	
							79		28	10	23	19	1	3	6	
S. ATLANTIC	9	*				3			1	10	4.0					
Del. Md.	2		0					2	6		1	2		*		
D.C.																
Va.	2	-				2		1	2		4	6			,	
W. Va.							. 2	1	5		2	1				
N.C.	1			*		1		1	3	6	7	- 1	-	-		
S.C. Ga.	1	*	-					1	3		2	9		1	2	
Fle.								N	N	3	6	1	1	2	3	
									-		-					
E.S. CENTRAL					2		- 15	1	7	-	2	-			1	
Ky.	,				2		. 3		3	-	1		-			
Tenn. Als.				-			. 5		2							
Miss.							. 2	1	2				*			
W.S. CENTRAL		23	30				. 13	1	8	1	10	10	2	1	11	
Ark.							. 1			1	9	1	-			
La. Okla.							. 3	N	N		1	2				
Tex.		23	30		-		- 16	1	8			6	2	7	1	
					3											
MOUNTAIN		1 1	18	-	-		1 11	3	42	20	32 17	10		3		
Mont.							: 1	2	3	16	1			1		
Idaho							. 1	2	3		1			- 1		
Wyo. Colo.							1 6			. 2	11	4				
N. Mex.							- 1	N	N	1 1	2	4				
Ariz.		1 -					- 1	1	37							
Utah		- 1	18				- 2		1		1	1		2		
Nev.																
PACIFIC	2		. 1			2	5 35		61		14	. 4	1 1	20	3	
Wash.		2 .					- 2		12	- 1	6					
Oreg.		1 .					1 8	N	- 1		4	,				
Calif.	2	3 U	1 1	7 U	3	2	3 23	U	45		4		U		2	
Alaska					2		1 2		3				. 1	1		
Hawreii		2 .							,							
Guerri		- U	1	- U				U		- U			- U	*		
P.R.		2 .					1 -	4					1 -	1		
V.L				:			5 -									
Pac. Trust Terr.		- U		- U				U		- U			- U			

^{*}For messies only, imported cases includes both out-of-state and international importations.

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending February 11, 1984 and February 12, 1983 (6th Week)

Reporting Area	Syphilis ((Primary & 5	(Civilien) Secondary)	Toxic- shock Syndrome	Tuber	culceis	Tulu- remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies Anima	
	Cum. 1984	Cum. 1984 Cum. 1983		Cum. 1984	Cum. 1983	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1984	
UNITED STATES	3,095	4,019	2	1,920	2,190	8	21	8	398	
NEW ENGLAND	81	101		60	40	-		*	2	
Maine N.H.	1	i		5	4				2	
/t.		1		1	3	-		-	-	
Mass.	48	70		24	14		-			
R.I. Conn.	28	27		10	14			2		
MID ATLANTIC	404	436	*	388	421		2	-	31	
Jipstate N.Y. N.Y. City	27	27 283		55 153	79 169	-	1		1	
V.J.	85	84	-	87	94	-	1		1	
Pa.	62	62		93	89				30	
EN CENTRAL	118	222		266	349		4	1	17	
Dhio	31	54		64	58		2	1	2	
nd.	29	26	-	26	44	*	1		3	
N.	17	98	*	101	172	*			6	
Mich. Wis.	29 12	30 14	-	61 14	60 15	-	i	-	7	
WIN CENTRAL	59	46	1	51	67	4	1	2	55	
Minn,	12	24	i	8	5	-	1		7	
lowa	4	2		9	14		-		12	
Mo.	34	16		21	39	4	*	2	5	
N. Dak.	-	-		2					12	
S. Dak.	ā	í		1 5	2 2	-		*	11	
Nebr. Kans.	5	3		5	5				Ä	
S. ATLANTIC	985	1,029	1	451	424		2		130	
Del.	-	9		4	1		-			
Md.	45	61		68	29				89	
D.C.	31	47		9	15	-		-		
Va. W. Va.	55	74	1	33 17	25 20		1		25 3	
N.C.	93	103		69	30	-	-		3	
S.C.	93	83		64	49					
Ge.	175	170		54	87				12	
Fia.	488	480		133	168	-	1	-	1	
E.S. CENTRAL	224	274		179	232		2	2	14	
Ky.	10	17	*	40	69	-	2	:	3	
Tenn. Ale.	52 76	70 124		57 70	70 61	-	2	1	7	
Miss.	86	63		12	32					
W.S. CENTRAL	750	1,011		147	177	1	1	1	96	
Ark.	25	13		6	7			1	10	
La.	177	190		26	50		.1		-	
Okin. Tex.	526	777	:	103	32 88	1		-	10 76	
MOUNTAIN	70	86		31	72	3	2		14	
Mont.	70	2		31	6		1		9	
idaho	3	1		1	5					
Wyo.	1	2			2			-	-	
Calo.	10	20			5				- :	
N. Mex. Ariz.	27	28 18		17	14 36	i	1		1 4	
Utah	3	5		2	36	2	-			
Nev.	18	10		î	4					
PACIFIC	404	814		347	398		7		39	
Wash.	12	31	*	11	22	-				
Oreg.	13	9	-	17	19		-			
Calif. Alaska	366	761	U	282	325		7		38	
Hawaii	13	8	:	29	28		:	-		
Guam		-	U		1					
P.R.	126	84		27	70		1			
V.I.	2	1		-	-					
Pac. Trust Terr.			U				-			

TABLE IV. Deaths in 121 U.S. cities,* week ending February 11, 1984 (6th week)

	All Causes, By Age (Years)								A	All Causes, By Age (Years)					
Reporting Area	All Ages	>85	46-84	25-44	1-24	<1	Total	Reporting Area	All Ages	>65	45-64	25-44	1-24	<1	P&I* Tota
EW ENGLAND	737	531	135	37	13	21	71	S. ATLANTIC	1,425	870	347	111	46	51	6
ostan, Mess.	173	112	40	11	3	7	21	Atlanta, Ga.	145	85	35	10	7	8	1
ridgeport, Conn.	59	37	14	3	2	3	9	Baltimore, Md.	314	185	93	22	8	8	1
ambridge, Mass.	31	27	2	1	1		3	Charlotte, N.C.	81	53	14	10	1	3	
all River, Mass.	37	27	10	*	-		2	Jacksonville, Fla.	81 121	56 66	31	15	4	5	
artford, Conn.	64	45	9	9		1	3	Miami, Fla. Norfolk, Va.	62	37	18	3	3	1	
owell, Mess.	31	22	5	2	1	2	4	Richmond, Va.	66	41	12	7	3	3	
ynn, Mass.	27	20	5 4	1	- 1		2	Savannah, Ga.	48	28	13	4	2	1	
ew Bedford, Mass ew Haven, Conn.	48	38	6	3			*	St. Petersburg, Fla.	103	88	13		-	2	
rovidence, R.I.	93	71	17	1	1	3	10	Tampe, Fle.	65	37	14		3	5	
omerville, Mass.	10	6	4	1		-		Washington, D.C.	289	160	79	25	11	14	1
pringfield, Mess.	49	38				5	5	Wilmington, Del.	50	34	12	2	2		
Vaterbury, Conn.	41	31	7	3		-	2							-	
Vorgester, Mass.	47	36	6	2	3		10	E.S. CENTRAL	802	521	179	50	25	26	4
								Birmingham, Ala.	117	82	25	4 2	2	2	
	2,617	1,780	543	184	56	52	119	Chattanooga, Tenn.	53 79	37 55	12	4	3	4	
Albany, N.Y.	61	41	15	2	1	2	2	Knoxville, Tenn. Louisville, Ky.	101	69	24		1	4	
Allentown, Pa.	21	16	4	1		3	9	Memphis, Tenn.	202	127	49		5	4	1
luffalo, N.Y.	127	82 27	30	10	2 2	2	6	Mobile, Ala.	95	63	17	8	5	2	
Camden, N.J. Bizabeth, N.J.	38	23		3	4	-	3	Montgomery, Ala.	37	19	8		1	4	
irie, Pa.t	31	24	5	1	1	- 1	2	Nashville, Tenn.	118	69	31		4	6	
Jersey City, N.J.	56	37	13	3	1	2	-		****						
N.Y. City, N.Y.	1.569	1.071	310	130	30	28	61	W.S. CENTRAL	1,674	1,027	404		64	68	
Vawark, N.J.	80	42	19	8	6	3	6	Austin, Tex.	28	18	4	3	1	2	
aterson, N.J.	31	24	5	1		1	6	Baton Rouge, La.	36	18	9		2	2	
Philadelphia, Pa.†	110	67	33	3	2	5	6	Corpus Christi, Tex.	36	24	9	2		- 1	
Pittsburgh, Pa.f	61	40	17	1	2	1	3	Dollas, Tex.	240	142	61		10	11	
Reading, Ps.	35	30	4	1			2	El Paso, Tex.	70 90	39 52	17		2 4	6	
Rochester, N.Y.	129	87	26	11	3	2	7	Fort Worth, Tex. Houston, Tex.	646	380	180		26	21	
Schenectady, N.Y.	27	17	6	2	1	- 1	7	Little Rock, Ark.	63	40	15		10	3	
Stranton, Pa.1	30	23	7			1	4	New Orleans, La.	125	80	26		3	4	
Syracuse, N.Y. Trenton, N.J.	79	59 18	18	2	1	1	-	San Antonio, Tex.	202	140	33		6	5	
Utics, N.Y.	30	26	3	- 1			1	Shreveport, La.	46	32	6		-	3	
Yonkers, N.Y.	31	26	4	1			2	Tulsa, Okla.	92	62	20			4	
EN CENTRAL	2,404	1,706	417	114	75	80		MOUNTAIN	682	447	141			29	
Akron, Ohio	66	48	11	3	1	3		Albuquerque, N.Me		53	12			5	
Canton, Ohio	28	17	8	3			1	Colo. Springs, Colo		21	12			13	
Chicago, III 🚦	610	527	12	13	21	25		Benver, Colo. Las Vegas, Nev.	142	90 50	26			13	
Cincinnati, Ohio	148	99	35	6	3	5		Ogden, Utah	13	12	-				
Claveland, Ohio	199	120	52 36	15	6	6		Phoenia, Aria.	172	112	35	5 13	7	5	5
Columbus, Ohio Dayton, Ohio	137	85 72		5	4	2		Pueblo, Colo.	25	18	-				
Detroit Mich.	110	168	27 53	28	11	10	7	Salt Lake City, Utah	40	25	- 1	9 3	2	1	1
Evansville, Ind.	41	31	9	1			5	Tucson, Ariz.	100	66	16	8 7	7	4	l.
Fort Wayne, Ind.	51	32	13	2	1	3									
Gary, Ind.	13	4	4	2	2	1		PACIFIC	1,827	1,222	40	3 101	46	53	3
Grand Rapids, Mic		36	10		1	1		Berkeley, Calif.	16	13		1 1	1		-
Indianapolis, Ind.	178	112	45	7	6		3	Fresno, Calif.	66	47 18	1	1 6			-
Madison, Wis.	41	20	12	2	4	3		Glendale, Calif. Honolulu, Hawaii	74	47	2				3
Milwaukee, Wis.	160	113	32	9	4	2		Long Beach, Calif.	85	54					1
Peoria, III. Rockford, III.	36	24 25	10	2	1	1		Los Angeles, Calif.	489	338					3
South Bend, Ind.	37 55	42	9	2	i	2		Oakland, Calif.	71	43					3
Toledo, Ohio	106	79	18	3	2	- 4			35	29		6 .			
Youngstown, Ohi		52	13	4	1	7		Portland, Oreg.	126	84	3	4 8			2
W.N. CENTRAL	756	506	144	49	24	31	32	Sacramento, Calif. San Diego, Calif.	142	86	3	8 (3 6	3 4	4
Das Moines, lows	51	39	6	4	1	1		San Francisco, Cali	if. 167	106			2 7	1 14	
Duluth, Minn.	24	18	5	1				San Jose, Calif.	156	109		5 (2
Kansas City, Kans		20	7	1	2	1	3 2	Seattle, Wash.	149	93			8 2		0
Kenses City, Mo.	128	75	27		7		7	Spokane, Wash.	68	51		9 4			-
Lincoln, Nebr.	23	17	4		1		- 1		96	66	1	8 4	4 8		3
Minneapolis, Min		55	21		5		1 3		12,924	8,610	224	9 9/1	900	41	9
Omaha, Nebr.	- 84	60	14		2	- 1	2 3	TOTAL	12,924	8,510	2,71	3 80	8 360	3 41	5
St. Louis, Mo. St. Paul, Minn.	156	107	30		4										
	81		13	6	2		5 3								

^{*}Mortality data in this table are voluntarily reported from 121 cities in the United States, most of which have populations of 100,000 or more. A death is reported by the place of its occurrence and by the week that the death cartificate was filed. Fetal deaths are not included:

**Pinaumonia and influenza*

**Penaumonia and influenz

TABLE V. Years of potential life lost, deaths, and death rates, by cause of death, and estimated number of physician contacts, by principal diagnosis, United States

Cause of	Years of potential life lost before		nted mortality nmber 1983	Estimated number		
morbidity or mortality (Ninth Revision ICD, 1975)	age 65 by persons dying in 1982*	Number*†	Annual Rate/100,000*†	of physician contacts September 1983*		
ALL CAUSES (TOTAL)	9,429,000	157,500	818.6	102,500,000		
Accidents and adverse effects (E800-E949)	2,367,000	8,120	42.2	5,700,000		
Malignant neoplasms (140-208)	1,809,000	37,020	192.3	2,200,000		
Diseases of heart (390-398, 402, 404-429)	1,566,000	56,500	293.5	5,600,000		
Suicides, homicides (E950-E978)	1,314,000	4,230	22.0	_		
Cerebrovascular diseases (430-438)	256,000	12,200	63.4	800,000		
Chronic liver disease and cirrhosis (571)	252,000	2,140	11.1	100,000		
Pneumonia and influenza (480-487)	118,000	3,210	16.7	600,000		
Chronic obstructive pulmonary diseases and allied conditions (490-498)	114,000	4.410	22.9	1,200,000		
Diabetes mellitus (250)	106,000	2,950	15.3	2,700,000		
Prenatal care* Infant mortality*		3,200	10.4 /1,000	2,900,000 0 live births		

^{*}For details of calculation, see footnotes for Table V, MMWR 1984;33:2.

[†]National Center for Health Statistics, *Monthly Vital Statistics Report* (MVSR), Vol. 32, No. 10, January 24, 1983, pp. 8-9.

[§]IMS America National Disease and Therapeutic Index (NDTI), Monthly Report, September 1983, Section III.

MVSR Vol. 32, No. 9, December 28, 1983, p. 1.

Fulminant Hepatitis - Continued

In Kentucky, 17 outbreak-related cases occurred between January and September 1983. Twelve patients were rnale, and all 17 were white, non-Hispanic. Ages ranged from 18 to 30 years (median 22 years). Two of the 17 patients (one male, one female) had fulminant disease that resulted in death, for a CFR of 11.8%. Fifteen patients had needle exposures; two were sexual contacts of patients.

In California, 19 HB cases were identified between June and December 1983. Seventeen patients were male; 17 were Hispanic; one, an American Indian; and one, white, non-Hispanic. Ages ranged from 18 to 34 years (median 20.5). Three patients, all male (including two brothers), had fulminant HB that resulted in death, for a CFR of 15.8%. Eighteen patients had needle exposures; one was a sexual contact of a patient.

The combined outbreak-related CFR was 13.9%, as compared with a combined CFR of 4.5% in 22 concurrent nonoutbreak-related cases and a CFR of 1% expected for hospitalized HB patients.

In both outbreaks, the only hepatotoxin identified was alcohol; however, the alcohol intake of patients with fulminant HB did not differ significantly from that of patients with nonfulminant disease. Anti-Delta antibody was detected in one of three patients with fulminant HB from whom serum was still available and in none of 32 patients with nonfulminant HB. This patient had strongly positive IgM-anti-Delta and a biphasic clinical course indicating co-infection with the Delta agent. In addition, at least two hepatitis non-A, non-B (NANB) cases and several previous NANB cases were identified among intravenous-drug users in both outbreaks.

Reported by RL Schaefer, MS, Regional Medical Center, RL Wolfe, MD, CM Steinfeld, MD, EE Kawas, MD, DA Martin, MD, Hopkins County Health Dept, Madisonville, MW Hinds, MD, State Epidemiologist, Kentucky Dept of Health Svcs; RH Johnson, MD, Kern County Medical Center, Bakersfield, JR Hayes, MD, Jacobs, MD, Porterville, J Pendleton, Jr, MD, Tulare County Health Dept, AG Redeker, MD, Los Angeles, RR Roberto, MD, J Chin, MD, State Epidemiologist, California Dept of Health Svcs; Hepatitis Br, Div of Hepatitis and Viral Enteritis, Center for Infectious Diseases, CDC.

Editorial Note: Hepatitis B is generally a mild disease with a CFR of only 1% in patients ill enough to require hospitalization. In one large, drug-related military outbreak, no deaths occurred among several thousand patients with clinical HB (1). The severity of the current outbreaks might be explained by any of several factors, including an unusually virulent strain of HB, simultaneous infection with other hepatotrophic viruses (NANB virus or the Delta agent) or the action of hepatotoxic chemicals. Although the existence of virulent strains of HB virus have not been clearly documented, each of the other factors has been implicated as a cause of at least one severe hepatitis outbreak.

One previously reported cluster of fulminant HB deaths among parenteral drug users, in which six of nine patients died, occurred in New Bern, North Carolina, in 1979 (2). An extensive investigation implicated the injection of 3,4 methylene diamphetamine (MDA) as a possible co-factor to account for the severity of the outbreak. Follow-up studies in chimpanzees exposed to MDA and HB virus were inconclusive. Two cases of NANB hepatitis in drug users were also associated with the outbreak.

There was no MDA use in either of the two current outbreaks. Although "crank," a locallyproduced, amphetamine-like substance, was available in California, it was used to a far lesser extent than heroin, and none of the patients with fulminant HB were known to have used it.

As in the New Bern outbreak, a few cases of NANB hepatitis were associated with both recent outbreaks. NANB hepatitis virus has been implicated, along with HB, in an exceptionally virulent outbreak of hepatitis (11 deaths/42 patients) among hemodialysis patients and staff in Edinburgh, Scotland, in 1969-1970, when stored sera were recently retested using modern serodiagnostic techniques for hepatitis A and B (3). However, until a reliable serologic

Fulminant Hepatitis - Continued

test for NANB virus(es) is developed, the role of concurrent NANB hepatitis infection in outbreaks of severe HB cannot be clearly defined.

Infection with the Delta agent was recently implicated as the cause of an exceptionally severe hepatitis epidemic among Venezuelan Indians (in which 34 of 149 patients died) (4). The Delta agent is an HB-dependent virus composed of a protein antigen (Delta antigen) and a ribonucleic acid (RNA) of low molecular weight, coated with hepatitis B surface antigen. It is transmissible as an independent infectious agent but may only replicate in the presence of active hepatitis B virus infection (5). Coprimary infection with HB/Delta, or Delta virus superinfection of an HB carrier may cause acute and/or chronic hepatitis; both types of infection have been associated with fullminant hepatitis B in Europe (6). Delta agent infection is endemic in southern Italy and in certain parts of South America and western Africa, but has been limited to hemophilia patients and drug-addict populations in the rest of Western Europe, North America, and Australia (7,8).

Evidence of infection with the Delta agent was found in one of three patients with fulminant HB in whom serum was available for testing (1/1 from California, 0/2 from Kentucky). Although Delta was not clearly defined as the cause of these outbreaks, testing for markers of Delta infection is indicated in any outbreak of fulminant hepatitis.

Control of hepatitis B outbreaks in parenteral-drug-using populations is difficult. Efforts in these outbreaks were focused on physician education with respect to diagnosis of HB by appropriate serotesting and prophylaxis of needle and sexual contacts of patients. Seronegative needle contacts should be offered HB vaccine in addition to standard passive prophylaxis. The Delta agent is transmitted similarly to HB and requires no special precautions other than those recommended for HB.

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Current Trends

Tuberculosis - United States, 1983

In 1983, a provisional total of 23,532 tuberculosis cases was reported to CDC, a 7.8% decrease from the 1982 final total of 25,520 cases. In 1968-1978, the average annual decrease in U.S. tuberculosis cases was 5.6%. However, in 1979-1981, when there was a large influx of Indochinese refugees, the average annual decline was 1.4%. From 1981 to 1982, the number of cases decreased by 6.8%.

Deaths from tuberculosis continue to occur. For 1982, the provisional estimate of tuberculosis deaths was 1,980, based on a 10% sample of death certificates by the National

Tuberculosis - Continued

Center for Health Statistics. This was similar to the final totals of 2,012 and 1,978 deaths in 1979 and 1980, respectively, but was higher than the 1981 provisional estimate of 1,780 deaths.

Reported by Div of Tuberculosis Control, Center for Prevention Svcs, CDC.

Editorial Note: Three factors may have contributed to the decreased number of tuberculosis cases reported in 1983: (1) a larger number of states began using the new national individual case reporting system, which requires more accurate verification of cases before they are counted; (2) the number of refugees arriving with tuberculosis in the United States from around the world declined, as did tuberculosis among Indochinese refugees, all of whom were screened for tuberculosis oversess. Indochinese refugees with tuberculosis have been completing supervised, directly observed chemotherapy before immigrating to the United States; and (3) the number of indigenous tuberculosis cases may have actually declined.

In 1979-1982, the average annual number of tuberculosis deaths was nearly 2,000. Tuberculosis was the leading cause of death among 38 communicable diseases for which mortality data were reported to CDC in 1979 (1). In fact, the number of tuberculosis deaths in 1979 exceeded the combined total for the other 37 communicable diseases. The number of tuberculosis deaths has shown essentially no decline in 1979-1982. Further analysis of tuberculosis mortality is under way.

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Update: Influenza Activity - United States

Influenza type A(H1N1) virus has now been reported from sporadic cases or outbreaks in all regions of the country except the northwest Pacific states (Figure 3). In contrast, influenza B virus has been isolated primarily in the western half of the country, as well as in parts of the northeast (Figure 4). As previously indicated (1), in those regions where circulation of both viruses is occurring, mixed outbreaks have now been confirmed. In Texas, types A(H1N1) and B viruses have been isolated from students at four colleges where outbreaks have been occurring, and similar results have been reported from at least one school outbreak each in Illinois and Wyoming. Other locations where approximately equivalent numbers of influenza types A(H1N1) and B viruses have been isolated from recent community activity include Honolulu, Hawaii, and Houston, Texas.

The elderly have been infrequently reported in this season's influenza outbreaks. In Utah County, Utah, a single influenza type B virus was isolated from an outbreak affecting eight of 79 residents in one nursing home late in January. Further laboratory studies are pending. In addition, no consistent elevation of deaths attributed to pneumonia and influenza in the 121 reporting cities has been seen through the end of January. Influenza A(H3N2) virus remains generally dormant; however, during January, sporadic isolates were reported in Alaska, Arizona, Massachusetts, Minnesota, New Mexico, Pennsylvania, Tennessee, and Texas.

Reported by P Glezen, MD, Baylor University School of Medicine, Houston, J Taylor, MPH, Texas Dept of Health: J Miner, MD, Utah County Health Dept, B Haslam, CR Nichols, Utah Dept of Health; State Epidemiologists and Laboratory Directors; Statistical Svcs Activity, Influenza Br, Div of Viral Diseases, Center for Infectious Diseases, CDC.

Reference

1. CDC. Update: influenza activity-United States. MMWR 1984;33:51-2.

Influenza - Continued

FIGURE 3. States with outbreaks or sporadic cases of influenza type A(H1N1) virus — United States, through February 10, 1984

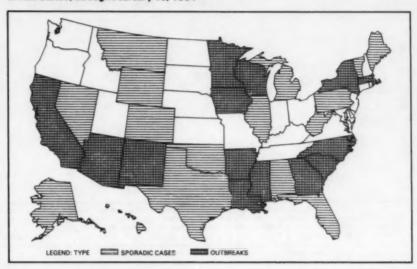
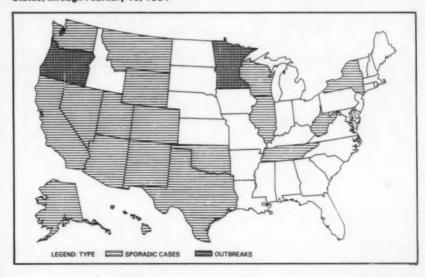


FIGURE 4. States with outbreaks or sporadic cases of influenza type B virus — United States, through February 10, 1984



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The editor welcomes accounts of interesting cases, outbreaks, environmental hazards, or other public health problems of current interest to health officials. Such reports and any other matters pertaining to editorial or other textual considerations should be addressed to: ATTN: Editor, Morbidity and Mortality Weekly Report, Centers for Disease Control, Atlanta, Georgia 30333.

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